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Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology
Office of Pharmacovigilance and Epidemiology

Pediatric Postmarketing Pharmacovigilance Review

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Product Name:	Amzeeq (minocycline) topical foam
Pediatric Labeling Approval Date:	October 18, 2019
Application Type/Number:	NDA 212379
Applicant:	Journey Medical Corp.
TTT Record ID:	2023-5790

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EXECUTIVE SUMMARY

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Amzeeq (minocycline) topical foam in pediatric patients less than 17 years of age. The Division of Pharmacovigilance (DPV) conducted this review in accordance with the Pediatric Research Equity Act (PREA). This review focuses on serious unlabeled adverse events associated with Amzeeq in pediatric patients.

Amzeeq (minocycline) topical foam is a tetracycline class drug that was initially approved in the U.S. on October 18, 2019. Amzeeq is currently indicated for the treatment of inflammatory lesions of non-nodular moderate to severe acne vulgaris in patients 9 years of age and older.

This pediatric postmarketing safety review was prompted by the pediatric labeling at initial FDA approval for Amzeeq that included a pediatric indication. The safety and effectiveness of Amzeeq have not been established in pediatric patients younger than 9 years. A pediatric safety review for Amzeeq has not been previously presented to the Pediatric Advisory Committee.

DPV reviewed all serious FAERS reports with Amzeeq in pediatric patients less than 17 years of age through July 30, 2023, and identified one report. However, this report was excluded from further discussion as it did not describe Amzeeq exposure.

There were no new safety signals identified, no increased severity or frequency of any labeled adverse events, and no deaths directly associated with Amzeeq in pediatric patients less than 17 years of age.

DPV did not identify any new pediatric safety concerns for Amzeeq at this time and will continue routine pharmacovigilance monitoring for Amzeeq.

1 INTRODUCTION

This review evaluates FDA Adverse Event Reporting System (FAERS) reports for Amzeeq (minocycline) topical foam in pediatric patients less than 17 years of age. The Division of Pharmacovigilance (DPV) conducted this review in accordance with the Pediatric Research Equity Act (PREA). This review focuses on serious unlabeled adverse events associated with Amzeeq in pediatric patients.

1.1 PEDIATRIC REGULATORY HISTORY

Amzeeq (minocycline) topical foam is a tetracycline class drug that was initially approved in the U.S. on October 18, 2019. Amzeeq is currently indicated for the treatment of inflammatory lesions of non-nodular moderate to severe acne vulgaris in patients 9 years of age and older.[1]

This pediatric postmarketing safety review was prompted by the original approval for Amzeeq that included a pediatric indication.[1] Support for the safety and effectiveness of Amzeeq came from three adequate and well controlled trials in pediatric patients aged 9 years and older and one pharmacokinetics study. The safety and effectiveness of Amzeeq have not been established in pediatric patients younger than 9 years. A pediatric safety review for Amzeeq has not been previously presented to the Pediatric Advisory Committee.

1.2 RELEVANT LABELED SAFETY INFORMATION

The Amzeeq labeling contains the following safety information excerpted from the Highlights of Prescribing Information and the *Pediatric Use* subsection. For additional Amzeeq labeling information, please refer to the full prescribing information.[1]

_____ CONTRAINDICATIONS _____

This drug is contraindicated in persons who have shown hypersensitivity to any of the tetracyclines or any of the ingredients within AMZEEQ. (4)

_____ WARNINGS AND PRECAUTIONS _____

- The propellant in AMZEEQ is flammable. Instruct the patient to avoid fire, flame, and smoking during and immediately following application. (5.1)
- The use of tetracycline-class of drugs orally during the second and third trimesters of pregnancy, infancy and childhood up to the age of 8 years may cause permanent discoloration of the teeth (yellow-gray-brown) and reversible inhibition of bone growth. (5.2, 5.3, 5.4, 8.1, 8.4)
- If *Clostridioides difficile* associated diarrhea occurs, discontinue AMZEEQ. (5.5)
- If liver injury is suspected, discontinue AMZEEQ. (5.6)
- If renal impairment exists, oral minocycline doses may need to be adjusted to avoid excessive systemic accumulations of the drug and possible liver toxicity. (5.7)
- Oral minocycline may cause central nervous system side effects including lightheadedness, dizziness, or vertigo. (5.8)
- Oral minocycline may cause intracranial hypertension in adults and adolescents. Discontinue AMZEEQ if symptoms occur. (5.9)
- Oral minocycline has been associated with autoimmune syndromes; discontinue AMZEEQ immediately if symptoms occur. (5.10)
- Photosensitivity can occur with oral tetracycline. Patients should minimize or avoid exposure to natural or artificial sunlight. (5.11)

- Oral minocycline has been associated with anaphylaxis, serious skin reactions, erythema multiforme, and DRESS syndrome. Discontinue AMZEEQ immediately if symptoms occur. (5.12)

_____ ADVERSE REACTIONS _____
The most commonly observed adverse reaction is headache. (6.1)

8.4 Pediatric Use
The safety and effectiveness of AMZEEQ have been established in pediatric patients 9 years of age and older for the treatment of inflammatory lesions of non-nodular moderate to severe acne vulgaris. Use of AMZEEQ for this indication is supported by three adequate and well controlled 12-week trials in patients 9 years of age and older; two of the trials included a 40-week open-label extension. Additional data was obtained from a 7-day open-label safety and pharmacokinetics study conducted in 20 patients 10 years to less than 17 years of age with acne vulgaris [see Clinical Pharmacology (12.3) and Clinical Studies (14)]. A total of 686 subjects 9 years of age and older received AMZEEQ in these clinical trials.

Safety and effectiveness for this indication have not been established in pediatric patients less than 9 years of age. The use of oral tetracycline drugs during tooth development below the age of 8 years may cause permanent discoloration of the teeth (yellow-gray-brown) and inhibition of bone growth [see Warnings and Precautions (5.2, 5.3)].

2 METHODS AND MATERIALS

2.1 FAERS SEARCH STRATEGY

DPV searched the FAERS database with the strategy described in **Table 1**.

Table 1. FAERS Search Strategy*	
Date of search	July 31, 2023
Time period of search	All dates through July 30, 2023
Search type	Drug Safety Analytics Dashboard (DSAD) Quick Query
Product terms	Product Name: Amzeeq NDA: 212379
MedDRA search terms (Version 26.0)	All Preferred Terms
* See Appendix A for a description of the FAERS database. Abbreviations: MedDRA=Medical Dictionary for Regulatory Activities, NDA= new drug application	

3 RESULTS

3.1 FAERS

3.1.1 Total Number of FAERS Reports by Age

Table 2 presents the number of adult and pediatric FAERS reports through July 30, 2023, with Amzeeq.

Table 2. Total Adult and Pediatric FAERS Reports* Received by FDA Through July 30, 2023, With Amzeeq			
	All Reports (U.S.)	**Serious† (U.S.)**	**Death (U.S.)**
Adults (≥ 17 years)	11 (9)	8 (6)	0 (0)
Pediatrics (0 - < 17 years)	2 (2)	1 (1)	1 (1)

* May include duplicates and transplacental exposures, and have not been assessed for causality

† For the purposes of this review, the following outcomes qualify as serious: death, life- threatening, hospitalization (initial or prolonged), disability, congenital anomaly, required intervention, or other serious important medical events.

3.1.2 Selection of U.S. Serious Pediatric Cases in FAERS

Our FAERS search retrieved one serious pediatric report through July 30, 2023. We reviewed the FAERS pediatric report with a serious outcome. We excluded the singular report from the case series as it did not describe events related to Amzeeq.[a]

3.1.3 Summary of Fatal Pediatric Cases (N=0)

There are no fatal pediatric adverse event cases for discussion.

3.1.4 Summary of Serious Non-Fatal Pediatric Cases (N=0)

There are no non-fatal pediatric adverse event cases for discussion.

4 DISCUSSION

DPV reviewed all serious FAERS reports with Amzeeq in pediatric patients less than 17 years of age through July 30, 2023, and identified one report. However, this report was excluded from further discussion.

There were no new safety signals identified, no increased severity or frequency of any labeled adverse events, and no deaths directly associated with Amzeeq in pediatric patients less than 17 years of age.

5 CONCLUSION

DPV did not identify any new pediatric safety concerns for Amzeeq at this time and will continue routine pharmacovigilance monitoring for Amzeeq.

6 REFERENCES

1. Amzeeq (minocycline) topical foam [Prescribing information]. Bridgewater, NJ; Vyne Pharmaceuticals, Inc.: July, 2021.

[a] The excluded FAERS report described a fatal outcome. The death was not attributed to Amzeeq as the patient was not exposed to this product.

7 APPENDICES

7.1 APPENDIX A. FDA ADVERSE EVENT REPORTING SYSTEM (FAERS)

The FDA Adverse Event Reporting System (FAERS) is a database that contains information on adverse event and medication error reports submitted to FDA. The database is designed to support FDA's postmarketing safety surveillance program for drug and therapeutic biological products. The informatic structure of the database adheres to the international safety reporting guidance issued by the International Council on Harmonisation. Adverse events and medication errors are coded to terms in the Medical Dictionary for Regulatory Activities terminology. The suspect products are coded to valid tradenames or active ingredients in the FAERS Product Dictionary.

FAERS data have limitations. First, there is no certainty that the reported event was actually due to the product. FDA does not require that a causal relationship between a product and event be proven, and reports do not always contain enough detail to properly evaluate an event. Further, FDA does not receive reports for every adverse event or medication error that occurs with a product. Many factors can influence whether an event will be reported, such as the time a product has been marketed and publicity about an event. Therefore, FAERS data cannot be used to calculate the incidence of an adverse event or medication error in the U.S. population.

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